

## REMARKS

Claims 10-25, 27, 32-34, 66-68, and 70 are pending in this application. Claims 16-24 are withdrawn. Claims 10, 27, and 34 are amended to correct informalities and for further clarity. The phrase "having a size of 8 to 13 amino acids" added to claim 10 is supported by original specification (see, for example, specification WO 97/40156 A1, page 10 lines 1-2). No new matter has been introduced. Reconsideration and allowance of the claims earnestly are requested.

### Priority Claim

Applicants thank the Examiner for granting the priority benefit from the parent application 08/635,344, filed April 19, 1996. To correct the informalities, applicants amend the first line of the specification by inserting priority claims to parent applications.

### Obviousness Rejections

At the outset, applicants note that the Examiner must show all of the recited claim elements in the combination of references that make up the rejection. When combining references to make out a *prima facie* case of obviousness, the examiner is obliged to show by citation to specific evidence in the cited references that (i) there was a suggestion to make the combination and (ii) there was a reasonable expectation that the combination would succeed. Both the suggestion and reasonable expectation must be found within the prior art, and not be gleaned from applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); see also MPEP §§ 2142-43.

When an examiner alleges a *prima facie* case of obviousness, such an allegation can be overcome by showing that (i) there are elements not contained in the references or within the general skill in the art, (ii) the combination is improper (for example, there is a teaching away or no reasonable expectation of success) and/or (iii) objective indicia

of patentability exist (for example, unexpected results). See *U.S. v. Adams*, 383 U.S. 39, 51-52 (1966); *Gillette Co. v. S.C. Johnson & Son, Inc.*, 16 USPQ2d 1923, 1927 (Fed. Cir. 1990); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 230 USPQ 416, 419-20 (Fed. Cir. 1986). Applicants submit that the rejections do not meet this test.

On pages 2-6, items 6-7 of the Office Action, the Examiner has maintained rejections of claims 10-15, 27, and 32 allegedly as unpatentable over Van Elsas *et al.* or Gjertsen *et al.* in view of Ruppert *et al.* or U.S. Patent No. 5,861,372. Applicants respectfully disagree with the Examiner. Applicants refer to the arguments made in response to paper nos. 16 and 23 and additionally note the following:

Van Elsas *et al.* provide p21ras-derived peptides of 9 and 11 mer in size (see Van Elsas *et al.* page 391 Table I) and experiments to bind of the peptides to HLA-A\*0201. Van Elsas *et al.* failed to induce CTL using 9 mer peptides (see Van Elsas *et al.* page 394 column 1, describing "not yet been able to induce responses"). Accordingly, the skilled artisan would have no reason to look to Van Elsas *et al.*, and thus there is no suggestion to make any combination involving Van Elsas in order to achieve the instant invention. On the contrary, instant invention provides 8-13 mer peptides that are able to induce CTL (see, for example, specification WO 97/40156 A1, page 10 lines 1-2; Examples 2-8 on Pages 30-48). Thus, Van Elsas *et al.* do not motivate the skilled artisan in any way to obtain the instant invention.

Gjertsen *et al.* provide a number of 17 mer peptides (see Gjertsen *et al.* Table I on page 451), however, experimental findings would not (see Gjertsen *et al.* Tables II-IV on pages 451-452) motivate others to use the disclosed peptides because the authors specifically indicated in conclusion that "the study [ ] do not allow any conclusions regarding the tumour response to ras peptide vaccination" (see Gjertsen *et al.* page 452, right column, conclusion paragraph 3). Therefore, Gjertsen *et al.* provide no incentive to the skilled artisan to rely upon its techniques.

Moreover, as indicated above, Gjertsen *et al.* used 17 mer peptides (see Gjertsen *et al.* Table I on page 451), in contrast, according to the invention, mutant *ras* peptides of the present invention "having a size of 8 to 13 amino acids" (see, for example, specification WO 97/40156 A1, page 10 lines 1-2). Thus, the size of the peptides of the instant invention is over 20% smaller than the peptides disclosed by Gjertsen *et al.*

On page 4 of the office action, the Examiner states that Ruppert *et al.* "teaches that an N-terminal tyrosine can increase HLA-A2 binding" and concluded that "in combination with Van Elsas *et al.* or Gjertsen *et al.* teaches the peptide of the instant claims." Applicants respectfully disagree and point out that Van Elsas *et al.* and Gjertsen *et al.* do not teach peptides of the instant invention, as described above and per currently amended claim 10. Therefore, any combination of the cited references does not make instant invention obvious.

On page 6, item 8 of the Office Action, the Examiner has maintained rejections of claims 25 and 66-67 allegedly as unpatentable over Van Elsas *et al.* or Gjertsen *et al.* in view of Ruppert *et al.* or U.S. Patent No. 5,861,372, as applied to claims 10-25, 27, and 32, and further in view of U.S. Patent No. 6,039,948. Applicants respectfully disagree with the Examiner. Applicants refer to the arguments made in response to paper nos. 16 and 23 and the arguments made above regarding items 6-7. Applicants further note that 6,039,948 does not rectify deficiencies of Van Elsas *et al.* or Gjertsen *et al.* in view of Ruppert *et al.* or U.S. Patent No. 5,861,372 to make the instant invention obvious. Withdrawal of the rejections is solicited.

On page 6, item 9 of the Office Action, the Examiner has maintained rejections of claims 33, 68, and 70 allegedly as unpatentable over Van Elsas *et al.* or Gjertsen *et al.* in view of Ruppert *et al.* or U.S. Patent No. 5,861,372, as applied to claims 10-25, 27, and 32, and further in view of U.S. Patent No. 5,800,810. Applicants respectfully disagree with the Examiner. Applicants refer to the arguments made in response to

paper nos. 16 and 23 and the arguments made above regarding items 6-7. Applicants point out that 5,800,810 does not rectify deficiencies of Van Elsas *et al.* or Gjertsen *et al.* in view of Ruppert *et al.* or U.S. Patent No. 5,861,372 to make the instant invention obvious. Withdrawal of the rejections is requested.

On pages 6-7, item 10 of the Office Action, the Examiner has maintained rejections of claims 34 allegedly as unpatentable over Van Elsas *et al.* or Gjertsen *et al.* in view of Ruppert *et al.* or U.S. Patent No. 5,861,372, as applied to claims 10-25, 27, and 32, and further in view of U.S. Patent No. 6,001,349. Applicants respectfully disagree with the Examiner. Applicants refer to the arguments made in response to paper nos. 16 and 23 and the arguments made above regarding items 6-7. Applicants indicate that 6,001,349 does not rectify deficiencies of Van Elsas *et al.* or Gjertsen *et al.* in view of Ruppert *et al.* or U.S. Patent No. 5,861,372 to make the instant invention obvious. Withdrawal of the rejections is earnestly requested.

Applicants submit that the above identified combination of references is nowhere supported by the references or in the common knowledge of the art. Accordingly, the rejection calls to mind the Federal Circuit decision of *In re Rouffet*, 149 F.3d 1350 (Fed. Cir. 1998), where the court explained:

As this court stated, "virtually all [inventions] are combinations of old elements." *Environmental Designs, Ltd. v. Union Oil Co.*, 713 F.2d 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983); *see also Richdel, Inc. v. Sunspool Corp.*, 714 F.2d 1573, 1579-80, 219 USPQ 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are combinations and mostly of old elements"). Therefore an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint to defeat the patentability of the claimed invention. Such an approach would be an "illogical and inappropriate process by which to determine patentability." *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1570, 38 USPQ2d 1551, 1554 (Fed. Cir. 1996).

To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventors and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.

*In re Rouffet*, 149 F.3d 1350, 1357 (Fed. Cir. 1998).

Applicants submit that the rejections do not satisfy the strictures of the *Rouffet* decision. The primary references are not combinable without proscribed hindsight. The secondary references do not rectify the deficient and contradictory teachings of the primary references, and therefore the obviousness rejection should be withdrawn.

#### **Definiteness Rejections**

Applicants thank the Examiner for withdrawing the rejections made under U.S.C. § 112, second paragraph. Applicants also amend claim 34 to obviate the new ground of rejection made on page 7, item nos. 11-13. Withdrawal of the rejection is requested.

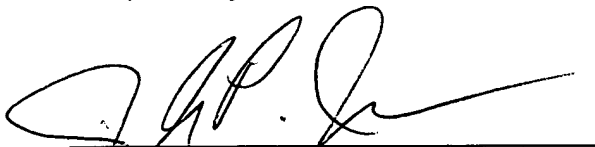
#### **Enablement Rejections**

On pages 7-8, item nos. 14-15 of the Office Action, the Examiner has rejected claims 10-15, 25, 27, 32-34, 66-68, and 70, under U.S.C. § 112, first paragraph. In response, applicants point out that the new ground of rejection is moot in view of currently amended claim 10, which recites "A mutant *ras* peptide having a size of 8 to 13 amino acids". Reconsideration and allowance is requested.

**CONCLUSION**

In view of the foregoing remarks and amendments, reconsideration of the application and allowance of the claims are requested. If any issues remain which the Examiner believes could be resolved through a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at 202-912-2777.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'J. Isacson', written over a horizontal line.

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Date

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